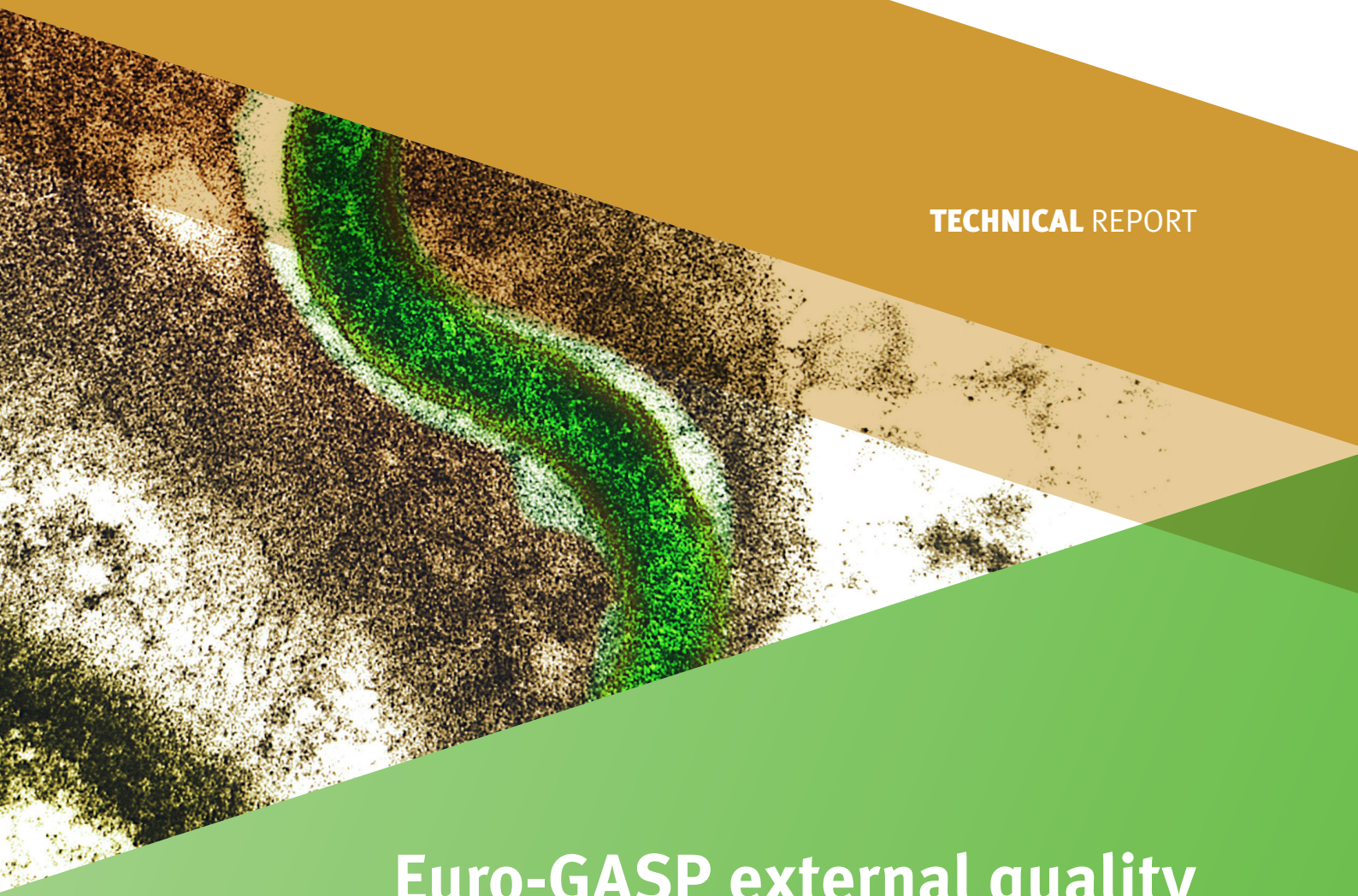

TECHNICAL REPORT

Euro-GASP external quality assessment scheme for *Neisseria gonorrhoeae* antimicrobial susceptibility testing

2018

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2018

This report was commissioned by the European Centre for Disease Prevention and Control (ECDC), coordinated by Gianfranco Spiteri and Andrew J Amato-Gauci and produced by Michaela Day and Michelle Cole, Public Health England, London, and Susanne Jacobsson and Magnus Unemo, Örebro University Hospital on behalf of the EURO-GASP network participants.

Suggested citation: European Centre for Disease Prevention and Control. Euro-GASP external quality assessment scheme for *Neisseria gonorrhoeae* antimicrobial susceptibility testing. Stockholm: ECDC; 2019.

Stockholm, September 2019

ISBN 978-92-9498-378-7
doi: 10.2900/802261
Catalogue number TQ-01-19-705-EN-N

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Abbreviations

AMR	Antimicrobial resistance
CLSI	Clinical and Laboratory Standards Institute
DSN	Dedicated surveillance network
EEA	European Economic Area
EQA	External quality assessment
ESSTI	European Surveillance of Sexually Transmitted Infections Project
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
Euro-GASP	European Gonococcal Antimicrobial Surveillance Programme
GC	Gonococcal
I	Intermediate
MIC	Minimum inhibitory concentration
PHE	Public Health England
R	Resistant
S	Susceptible
STI	Sexually transmitted infection
UK	United Kingdom
UKAS	United Kingdom Accreditation Service
UK NEQAS	United Kingdom National External Quality Assessment Service
WHO	World Health Organization

Executive summary

Introduction

External quality assessment (EQA) is an essential part of any laboratory-based surveillance system, allowing for the monitoring of performance and comparability of results from participating laboratories, identification of potential issues, and deployment of resources and training where necessary. An EQA scheme for antimicrobial susceptibility testing in *Neisseria gonorrhoeae* has been available to laboratories participating in ECDC's European Sexually Transmitted Infections (STI) surveillance network since 2010. This EQA scheme has so far shown high levels of interlaboratory comparability in the presence of differing methodologies. Problems identified previously included reduced comparability of results determined using discs diffusion compared with those determined by agar dilution and MIC gradient strip tests, media not suitably supporting gonococcal growth, and the use of MIC gradient strip tests from one manufacturer.

Materials and methods

The EQA specimen panel was selected by Public Health England (PHE) and distributed by the United Kingdom National External Quality Assessment Service (UK NEQAS). In October 2018, 27 laboratories in 26 participating countries received 10 gonococcal isolates for antimicrobial susceptibility testing. Of the 10 gonococcal isolates provided, one strain was in triplicate, and two strains were in duplicate to test intralaboratory concordance. The remaining isolates were all provided singularly, meaning that the *N. gonorrhoeae* antimicrobial susceptibility EQA panel comprised six different strains in total. The isolates chosen by PHE were representative of a range of different antimicrobial susceptibility profiles and consisted of the four WHO reference strains, WHO K, O, Q, Z, and two clinical isolates obtained in the UK in 2017. Participating laboratories were requested to test the EQA panel using local methodology (i.e. MIC gradient strip test, agar dilution or disc diffusion) and relevant international breakpoints (i.e. EUCAST, CLSI etc.) against a range of antimicrobial agents. Results were submitted directly to UK NEQAS who issued individual laboratory reports. The results were then supplied to PHE who decoded and analysed the results based on the categories of susceptibility assigned.

Results

Twenty-seven laboratories returned EQA results to UK NEQAS. Most laboratories used MIC gradient strip tests and EUCAST breakpoints. The highest level of categorical agreement (other than spectinomycin; 100%) was seen with ceftriaxone (98.6%), while the lowest was seen with azithromycin (77.6%).

Overall concordance decreased for most antimicrobials in comparison with the previous distribution, except for ciprofloxacin, which increased slightly from 94.1% to 98.1%. Overall, 95.2% and 99.4% of the reported minimum inhibitory concentrations (MICs) were within one (essential agreement) and two doubling dilutions of the modal MIC, respectively.

Discussion and conclusion

There has been further harmonisation of susceptibility testing methodologies and breakpoints used by participating laboratories; most laboratories used MIC gradient strip tests and all applied EUCAST breakpoints for interpretation of MIC results. Overall, the laboratories participating in the EQA scheme QA18 performed well and showed good levels of competency in testing *N. gonorrhoeae* isolates of unknown phenotype. Categorical agreement decreased slightly in this distribution when compared with 2017, with the exception of ciprofloxacin. The inter- and intralaboratory concordance was high in most cases, demonstrating comparability between different testing methodologies and allowing confidence in decentralised testing for surveillance purposes. Most susceptibility category discrepancies were attributable to strains with MICs on or close to a breakpoint, which highlights the need to consider the actual MIC as well as susceptibility category when interpreting susceptibility results. Analysis of the individual results submitted by the participating laboratories highlighted one centre in need of further guidance to help bring them into line with the Euro-GASP[1]-recommended target of 95% of MICs within two doubling-dilutions (fourfold) of the modal MICs and beta-lactamase assessment.

[1] European Gonococcal Antimicrobial Surveillance Programme

1 Introduction

The European Centre for Disease Prevention and Control (ECDC) is a European Union agency with a mandate to operate the dedicated surveillance networks (DSNs) and to identify, assess, and communicate current and emerging threats to human health from communicable diseases. Within its mission, ECDC shall:

> 'foster the development of sufficient capacity within the Community for the diagnosis, detection, identification and characterisation of infectious agents which may threaten public health. The Centre shall maintain and extend such cooperation and support the implementation of quality assurance schemes.' (Article 5.3, EC 851/2004[2]).

As part of its mandate, ECDC commissions and supports external quality assessment (EQA) exercises across public health microbiology laboratories in the EU/European Economic Area (EEA) Member States with the objective to:

- verify the quality and comparability of surveillance data reported at European level; and
- ensure threat detection capability for emerging and epidemic disease or drug resistance.

EQAs are conducted within a quality management system and evaluate the performance of laboratories. They are carried out by an outside agency and with materials supplied specially for this purpose. ECDC's disease-specific networks organise a series of EQAs for EU/EEA countries. In some networks, ECDC also includes non-EU/EEA countries in its EQA activities. The aim of these EQAs is to identify weak points in the diagnostic capacities of EU/EEA laboratories that are relevant to the surveillance of diseases listed in Commission Implementing Decision (EU) 2018/945; another aim is to ensure comparability of laboratory results from all EU/EEA countries.

The main purposes of EQA schemes include the following:

- Assessment of the general standard of performance ('state of the art')
- Assessment of the effects of analytical procedures (method principle, instruments, reagents, calibration)
- Evaluation of individual laboratory performance
- Identification and justification of vulnerabilities
- Providing continuing education for participating laboratories
- Identification of needs for training activities

A major aim of the European Sexually Transmitted Infections (STI) surveillance network is to strengthen the surveillance of *Neisseria gonorrhoeae* antimicrobial susceptibility in EU/EEA Member States. An EQA scheme for *N. gonorrhoeae* antimicrobial susceptibility testing was established in 2007 as part of the European Surveillance of STIs (ESSTI) programme funded by the Directorate-General for Health and Consumers (DG SANCO). The EQA has been part of the ECDC STI microbiology project since 2009, with the first ECDC EQA distributed in 2010.

The EQA scheme is available to all laboratories in the STI surveillance network. An EQA scheme is an essential component of the laboratory-based surveillance programme, ensuring comparability of data between and within testing centres, and successful performance in the EQA is a prerequisite for laboratories that want to participate in decentralised testing as part of antimicrobial resistance (AMR) surveillance across Europe [1,2].

Between 2010 and 2018, the number of laboratories participating in the *N. gonorrhoeae* antimicrobial susceptibility testing EQA increased from 18 to 27; in general, the EQA revealed high levels of interlaboratory comparability despite the presence of different antimicrobial susceptibility testing methodologies. Problems identified in previous EQA distributions included reduced comparability of results determined using discs diffusion compared with those determined by agar dilution and MIC gradient strip tests, media not suitably supporting gonococcal growth, and reduced comparability of results among laboratories using MIC gradient strip tests from a particular manufacturer.

The United Kingdom National External Quality Assessment Service (UK NEQAS) collaborated with Public Health England (PHE) and Örebro University Hospital for the EQA described in this report. UK NEQAS is accredited by the United Kingdom Accreditation Service (UKAS) to ISO 17043 (conformity assessment – general requirements for proficiency testing). Participation in this EQA scheme for *N. gonorrhoeae* antimicrobial susceptibility provides a mechanism for laboratories in the network to meet the requirements of these standards.

[2] Regulation (EC) No 851/2004 of the European Parliament and of the Council of 21 April 2004 establishing a European Centre for Disease Prevention and Control

2 Materials and methods

2.1 Antimicrobial susceptibility testing external quality assessment panel

In October 2018, 27 laboratories in 26 countries received ten gonococcal isolates (QA18) for susceptibility testing from UK NEQAS. The isolates included in the panel were selected by Public Health England to demonstrate a range of susceptibility profiles for relevant therapeutic antimicrobial agents and consisted of three WHO reference gonococcal strains, WHO K, O and Z [3], the recently assigned WHO Q (which is the pharyngeal isolate from a male who failed treatment in the UK in 2018 [4]), and two clinical isolates from the UK isolated in 2017. To measure intralaboratory reproducibility, one of these strains was supplied in triplicate: Strain 5 (WHO Z, coded in the EQA as 4936/4939/4941); two strains were supplied in duplicate: Strain 1 (G-999, EQA codes 4932/4937) and Strain 4 (WHO O, EQA codes 4935/4938).

The remaining three strains were supplied as individual isolates: Strain 2 (WHO Q, EQA code 4933), Strain 3 (WHO K, EQA code 4934) and Strain 9 (G-1581, EQA code 4940). Therefore, six different strains were included in the distribution.

Participating laboratories tested the EQA panel of isolates, using their own routine methodologies against the following therapeutic antimicrobials where possible:

- Azithromycin
- Cefixime
- Ceftriaxone
- Ciprofloxacin
- Gentamicin
- Spectinomycin

Participating laboratories also tested the EQA panel of isolates for beta-lactamase production where possible.

The antimicrobials listed are those detailed in the ECDC instructions, external quality assessment v6 [5].

2.2 Susceptibility testing methods

The methodology and the clinical breakpoints/guidelines used for determining the category of susceptibility for each antimicrobial tested were requested. All laboratories participating in the QA18 EQA used the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints[2] (Table 1). Antimicrobial susceptibility testing results for each isolate were reported as a) category of susceptibility (resistant (R), intermediate (I), susceptible (S)), and b) minimum inhibitory concentration (MIC) for the gradient strip and agar dilution methods.

Table 1: EUCAST breakpoints

	MIC breakpoint (mg/L)		
	S ≤	**I**	**R >**
Azithromycin	0.25	0.5	0.5
Cefixime	0.125		0.125
Ceftriaxone	0.125		0.125
Ciprofloxacin	0.03	0.06	0.06
Spectinomycin	64		64

Note: 2018 breakpoints used; there are currently no EUCAST interpretive criteria for gentamicin[3]
The 2019 EUCAST breakpoints were released in January 2019; for 2019, SIR categories were removed for azithromycin and replaced with an epidemiological cut-off (ECOFF) value of 1 mg/L.

[3] http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_8.1_Breakpoint_Tables.pdf

2.3. Analysis and interpretation of the results

Raw results for the EQA were submitted by each participating laboratory directly to UK NEQAS for the production of individual laboratory reports. The results were also forwarded to PHE for further collated analysis.

For the analysis, all MIC results that fell between the MIC gradient strip full-dilution scale were rounded up to the next full MIC gradient strip dilution as this was the most commonly used testing method. The minimum, maximum and modal MIC for each strain was established. The number of MIC measurements within two MIC dilutions of the modal MIC and the number of MIC measurements above or below two MIC dilutions of the modal MIC for each strain were established.

A percentage of overall MIC concordance for each laboratory was calculated for the number of isolates within two doubling dilutions of the modal MIC from the total number of antimicrobials, including beta-lactamase from each laboratory. Essential agreement (MICs within one doubling dilution of the modal) was also examined and used as the basis for an overall MIC score for each participating laboratory. The overall MIC score for each laboratory was calculated based on minor and major faults in the MIC for ceftriaxone, azithromycin and ciprofloxacin. Where the MIC result matched the modal result, a score of five was assigned; a one MIC doubling dilution difference from the modal was considered a minor fault, and a score of four was given; a difference of two doubling dilutions from the modal MIC was classified as a major fault and given a score of one. An MIC greater than two doubling dilutions from the modal was classified as a very major fault, and a score of zero was given. The total score was then converted into a percentage of the maximum score achievable (150 = (10x5) + (10x5) + (10x5)).

Consensus categories of susceptibility (categorical agreement) for each strain tested (six in total in this distribution; consensus calculated from all isolates in the triplicate or duplicate sets) were calculated once all participating laboratories had reported results back. The 'consensus' was assigned to the category reported most often, irrespective of breakpoint criteria used. The overall concordance for each antimicrobial was established by taking the average of each strain's percentage concordance. The total categorical concordance score was calculated by assigning a score of five for results the same as the modal, four for a minor fault (susceptible or resistant miscategorised as intermediate or vice versa), three for a major fault (susceptible miscategorised as resistant), and one for a very major fault (resistant miscategorised as susceptible).

Intralaboratory concordance was examined using the triplicate (Strain 5) and two duplicate strains (Strains 1 and 4). All MIC results for these strains were assigned a score: zero if the same as the other results, one if one MIC doubling dilution different, two if two MIC doubling dilutions different, and five if greater than two MIC doubling dilutions different. These results were then averaged for the total number of results observed and given a percentage error score by comparison to the maximum score possible if there were no concordant results, i.e. 3.33 =((5+5+5)/3)+(5/2)+(5/2))/3). The closer to zero the score was, the more consistent the laboratory MIC test results were.

3 Results

3.1 QA18 panel strain characteristics

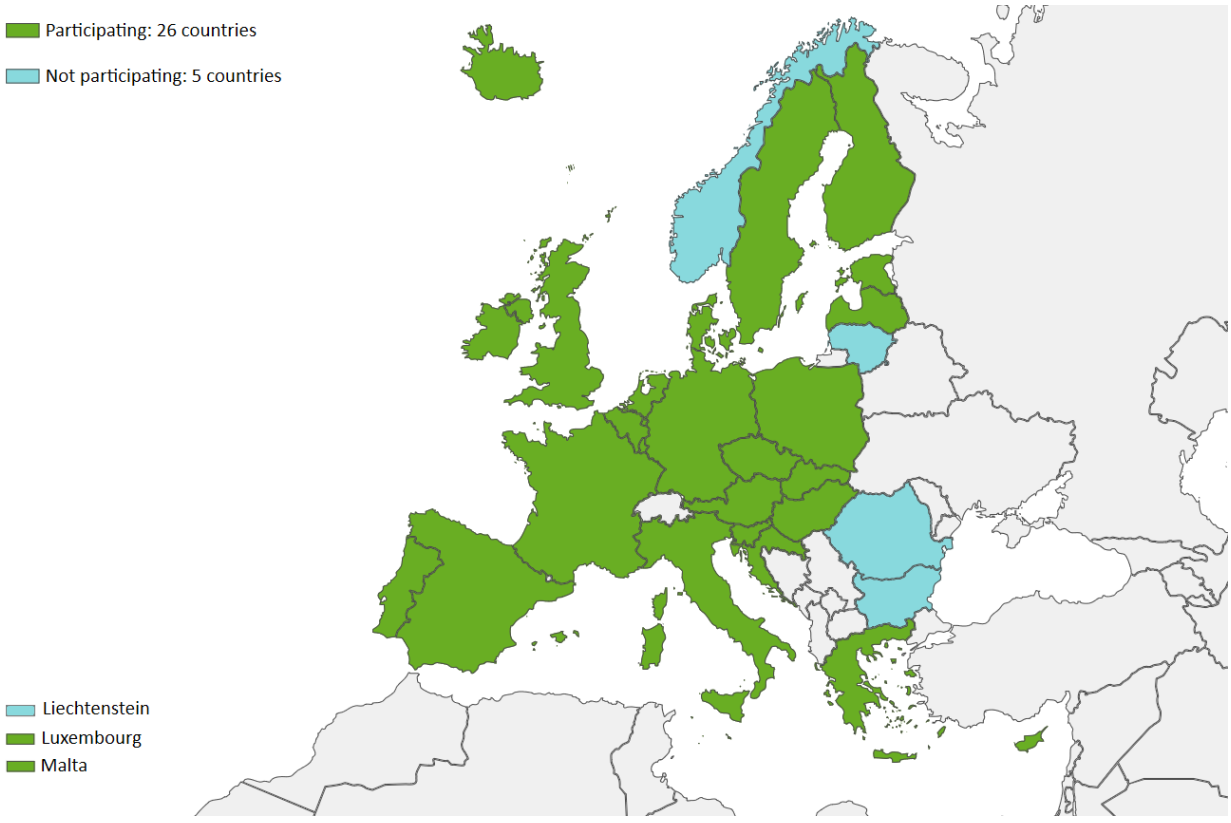
Table 2 shows the overall consensus category, the modal/range MIC for all tests, and the percentage concordance for each strain in the EQA panel. Consensus phenotypes for each strain tested are also shown. The strains tested demonstrated a range of phenotypes, and only one of the strains was fully susceptible to all antimicrobials tested (Strain 9, G-1581):

- Two strains were multi-resistant, with high-level resistance to ciprofloxacin; one also had high-level resistance to azithromycin and resistance to ceftriaxone (Strain 2, clinical isolate); one had moderate resistance to azithromycin and ceftriaxone (Strain 5, WHO Z).
- One strain had high-level resistance to ciprofloxacin and was susceptible to both azithromycin and ceftriaxone (Strain 3, WHO K).
- One strain was only resistant to ciprofloxacin (Strain 1, G-999).
- One strain was only resistant to spectinomycin (Strain 4, WHO O).

3.2 Susceptibility testing methods

Twenty-seven laboratories in 26 countries returned results to UK NEQAS (Figure 1). This is one country less than in the 2016 EQA as Norway did not perform any gonococcal susceptibility testing in 2018. All laboratories provided details on the methodology and breakpoints/guidelines (Table 3) used to test the isolates in the EQA. MIC gradient strip tests (96.4%) and GC agar (64.3%) were the most common testing methodology and medium used, respectively.

Figure 1: Countries participating in the 2018 *N. gonorrhoeae* susceptibility testing EQA scheme



Note: 27 laboratories participated in the 2018 EQA scheme; the United Kingdom had two participating laboratories.

Table 2: Consensus category, modal (range) MIC for gradient strip test and agar dilution (mg/L) and the percentage concordance of susceptibility category for the 2018 EQA panel

Strain		Azithromycin consensus	Cefixime consensus	Ceftriaxone consensus	Ciprofloxacin consensus	Gentamicin consensus	Spectinomycin consensus	Beta-lactamase consensus
Strain 1: 4932/4937 (G-999) CipR	Consensus category	S	S	S	R	N/A	S	POS
	Modal MIC (range)	0.125 (0.032-0.5)	≤0.016 (0.016-0.064)	≤0.016 (0.016-0.032)	0.5 (0.03-1)	4 (2-16)	16 (4-64)	-
	Susceptibility category concordance (%)	92.6	100	100	94.4	N/A	100	94
	Reference MIC	0.125	≤0.016	≤0.016	1	4	8	POS
Strain 2: 4933 (WHO Q) AzR, CfmR, CroR, CipR	Consensus category	R	R	R	R	N/A	S	NEG
	Modal MIC (range)	≥256	2 (1-4)	0.5 (0.25-2)	≥32 (4-32)	8 (2-8)	16 (4-64)	-
	Susceptibility category concordance (%)	100	100	100	100	N/A	100	100
	Reference MIC (3)	≥256	1	1	≥32	2	8	NEG
Strain 3: 4934 (WHO K) (3) CfmR, CipR	Consensus category	S	R	S	R	N/A	S	NEG
	Modal MIC (range)	0.25 (0.125-0.5)	0.25 (0.06-0.5)	0.064 (0.016-0.25)	≥32 (>0.06-32)	4 (2-8)	16 (8-64)	-
	Susceptibility category concordance (%)	63	73.1	96.3	100	N/A	100	100
	Reference MIC (3)	0.25	0.25	0.064	≥32	4	16	NEG
Strain 4: 4935 /4938 (WHO O (3) SpcR	Consensus category	S	S	S	S	N/A	R	POS
	Modal MIC (range)	0.25 (0.064-1)	0.016 (0.016-0.032)	0.016 (0.016-0.064)	0.008 (0.002-0.064)	4 (2-16)	≥1024 (16-1024)	
	Susceptibility category concordance (%)	55.6	100	100	94.4	N/A	100	96
	Reference MIC (3)	0.25	≤0.016	0.032	0.008	4	>1024	POS
Strain 5: 4936/4939/4941 (WHO Z) (3) AzR, CfmR, CroR, CipR	Consensus category	R	R	R	R	N/A	S	NEG
	Modal MIC (range)	1 (0.125-2)	1 (0.5-4)	0.5 (0.125-2)	≥32 (>0.06-32)	4 (2-8)	16 (2-64)	-
	Susceptibility category concordance (%)	54.3	100	95.1	100	N/A	100	92.3
	Reference MIC	1	2	0.5	≥32	4	16	NEG
Strain 6: 4940 (G-1581) Susceptible	Consensus category	S	S	S	S	N/A	S	NEG
	Modal MIC (range)	0.125 (0.032-0.25)	≤0.016	≤0.016	0.002 (0.002-0.064)	4 (2-16)	16 (4-64)	-
	Susceptibility category concordance (%)	100	100	100	100	N/A	100	100
	Reference MIC	0.125	≤0.016	≤0.016	0.004	4	8	NEG

** MICs taken from UK NEQAS reference MIC results*
Note: No consensus category of susceptibility was assigned to gentamicin as there are currently no published breakpoints for this antimicrobial.
N/A – not available

3.3 Interpretation of MICs

All 27 laboratories reported adherence to the EUCAST breakpoints[4,3] (Table 1). Most laboratories that tested gentamicin did not interpret categories of susceptibility as there are currently no internationally defined interpretive criteria for this antimicrobial. However, two laboratories did submit categories of susceptibility for gentamicin, using local interpretive criteria; these data were not analysed in this report.

Table 3: Susceptibility testing methods used by laboratories participating, October 2018 EQA

	Number of participating laboratories (27)
Type of susceptibility test used	
MIC gradient strip tests	26
Agar dilution	1
Testing guidelines used	
EUCAST[3]	27
Agar base used	
Chocolatised blood agar	11
GC agar base	9
Thayer-Martin/Mueller-Hinton	3
Diagnostic sensitivity agar	2
Other	2

3.4 Coded breakdown of concordance

Due to the confidential nature of the EQA scheme, only coded laboratory breakdowns for beta-lactamase assessment concordance, category of susceptibility concordance, MIC values determined by MIC gradient strip tests, and agar dilution are shown in Annex 1 (Tables A1.6–A1.12). An analysis of the breakdown of results showed that eight laboratories reported isolates with MICs greater than two doubling dilutions different from the modal MIC or submitted a beta-lactamase result different from the consensus. Only one laboratory reported more than 5% of results greater than two doubling dilutions from the modal MIC; it used diagnostic sensitivity agar. As this laboratory participates in the Euro-GASP sentinel surveillance via centralised testing, this will not have an impact on Euro-GASP data; the laboratory will, however, receive additional support to improve its susceptibility testing.

In the 2017 EQA (QA17), seven laboratories reported more than 5% of results greater than two doubling dilutions from the modal MIC. Six of the seven laboratories improved in the QA18 EQA and now have over 95% of results within two doubling dilutions of the modal MICs. This shows that the problems identified in QA17 have been rectified.

One of the seven laboratories, however, has not managed to reach the 95% threshold, but there was a marked improvement: from a concordance level of 85.1% (2017) to 92.5% (2018). The remaining issues appear to be with only one antibiotic: ciprofloxacin.

3.5 Susceptibility category concordance

Three laboratories submitted incomplete susceptibility category results.

Incomplete data were submitted for:

- cefixime (laboratory 95589: only isolate 4938) and
- ciprofloxacin (laboratory 92628: only isolate 4939; laboratory 92632: only isolate 4940).

Laboratory 95588 did not test for cefixime susceptibility.

Nineteen laboratories (Table A1.10) submitted complete datasets for spectinomycin, and 17 (Table A1.11) submitted complete data for gentamicin. Two laboratories (92629 and 95589) did not test for the production of beta-lactamases.

The highest levels of categorical agreement were seen for spectinomycin (100%) and ceftriaxone, with 98.6% concordance; the lowest level was seen for azithromycin, with 77.6% concordance (Figure 2 and Tables A1.1, A1.3,

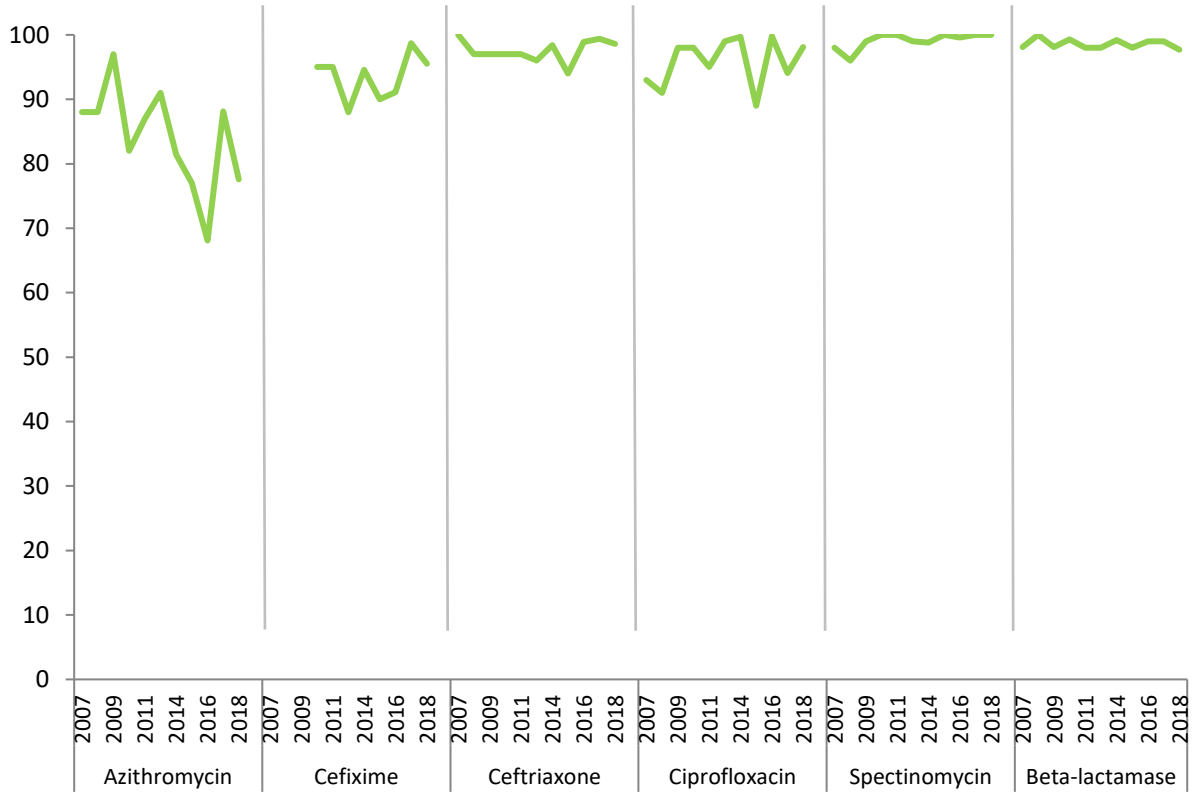
[4] http://www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Breakpoint_tables/v_8.1_Breakpoint_Tables.pdf

A1.5, A1.7, A1.9 and A1.12). Consensus susceptibility categories were not assigned for gentamicin as there are currently no published breakpoints. Three testing centres did not correctly identify beta-lactamase production; laboratory 90984 in one isolate (isolate 4935) (Table A1.12), laboratory 92625 in one isolate (isolate 4932), and laboratory 94937 in three isolates (the duplicates 4932 and 4937 and isolate 4938). One laboratory (94936) had false-positive results (isolates found beta-lactamase positive when beta-lactamase negative) for the strains in triplicate (4936, 4939, 4941).

When categorical agreement data are compared with previous EQA distributions from both ESSTI (QA2007, QA2008 and QA2009) [6] and ECDC Euro-GASP (QA2010–17) [7-13], there is a slight decrease in concordance for most antimicrobials tested (Figure 2). The exception is ciprofloxacin, which displayed a slight increase in concordance (98.1%) compared to 2017 (94.18%), and spectinomycin, which remained at 100% in 2018 as in the previous year.

Beta-lactamase result concordance remains high at 99% (Figure 2).

Figure 2: Longitudinal comparison of EQA interlaboratory antimicrobial categorical agreement, 2007–2018, EU/EEA



Note: Cefixime was added to the EQA scheme in 2010.
ESSTI EQA distributions (2007–2009) constituted 30 isolates (10 strains in triplicate).
The number of laboratories participating in the EQA changed over time: 19 laboratories (2007 and 2008), 16 laboratories (2009), 18 laboratories (2010), 20 laboratories (2011), 19 laboratories (2012), 21 laboratories (2014), 26 laboratories (2015), 27 laboratories (2016), 28 laboratories (2017), 27 laboratories (2018)

3.6 MIC concordance

Overall, MIC essential agreement (MIC results within one doubling dilution of the modal MIC recorded) was at 95.2% (Table 4) for all antimicrobials tested, showing an increase in concordance from the previous EQA panel distribution (87.7%) [13]. Highest MIC concordances were seen for cefixime (97.7%), while the lowest were seen for azithromycin (90.4%) (Table 4). For all MICs combined, 99.4% were within two doubling dilutions of the modal MIC. Ciprofloxacin had the highest proportion of isolates, with a MIC greater than two doubling dilutions of the modal MIC (2.2%), and cefixime, ceftriaxone and gentamicin had the lowest (0.0%).

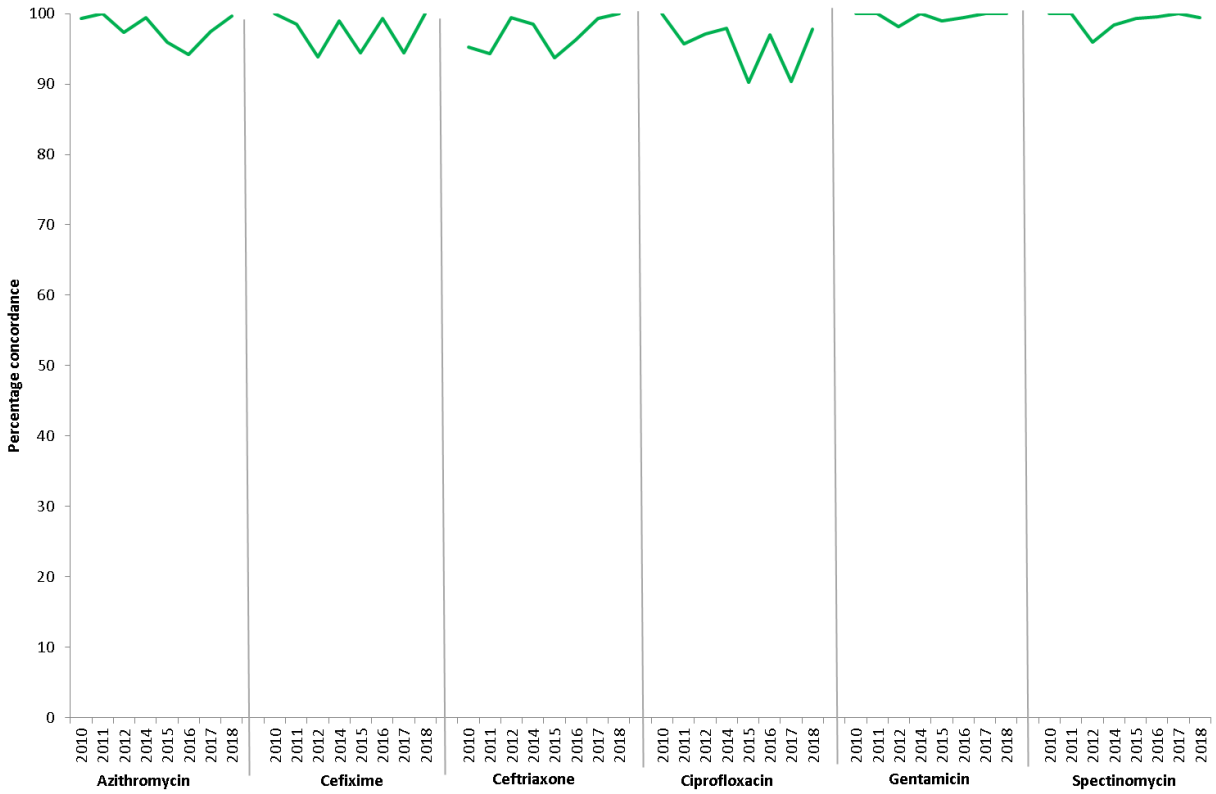
When MIC concordance data are compared with previous ECDC Euro-GASP EQA distributions (QA2010–17) [7-13], a slight increase in MIC concordance can be seen for most of the tested antimicrobials (Figure 3).

Table 4: Variation from modal MIC for EQA QA18

QA18	Azithromycin		Cefixime		Ceftriaxone		Ciprofloxacin		Gentamicin		Spectinomycin		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Within +/- 1 doubling dilution	244	90.4	253	97.7	260	96.3	263	98.1	158	92.9	183	96.3	1361	95.4
Within +/- 2 doubling dilutions	25	9.3	6	2.3	10	3.7	0	0.0	12	7.1	6	3.2	59	4.1
+/- >2 doubling dilutions	1	0.4	0	0.0	0	0.0	5	1.9	0	0.0	1	0.5	7	0.5
Total no. of isolates with MIC data	270		259		270		268		170		190		1427	

No.: Number of isolates with MIC data

Figure 3: Longitudinal comparison of EQA interlaboratory MIC concordance, percentage of results within two doubling dilutions of the mode, 2010–2018, EU/EEA

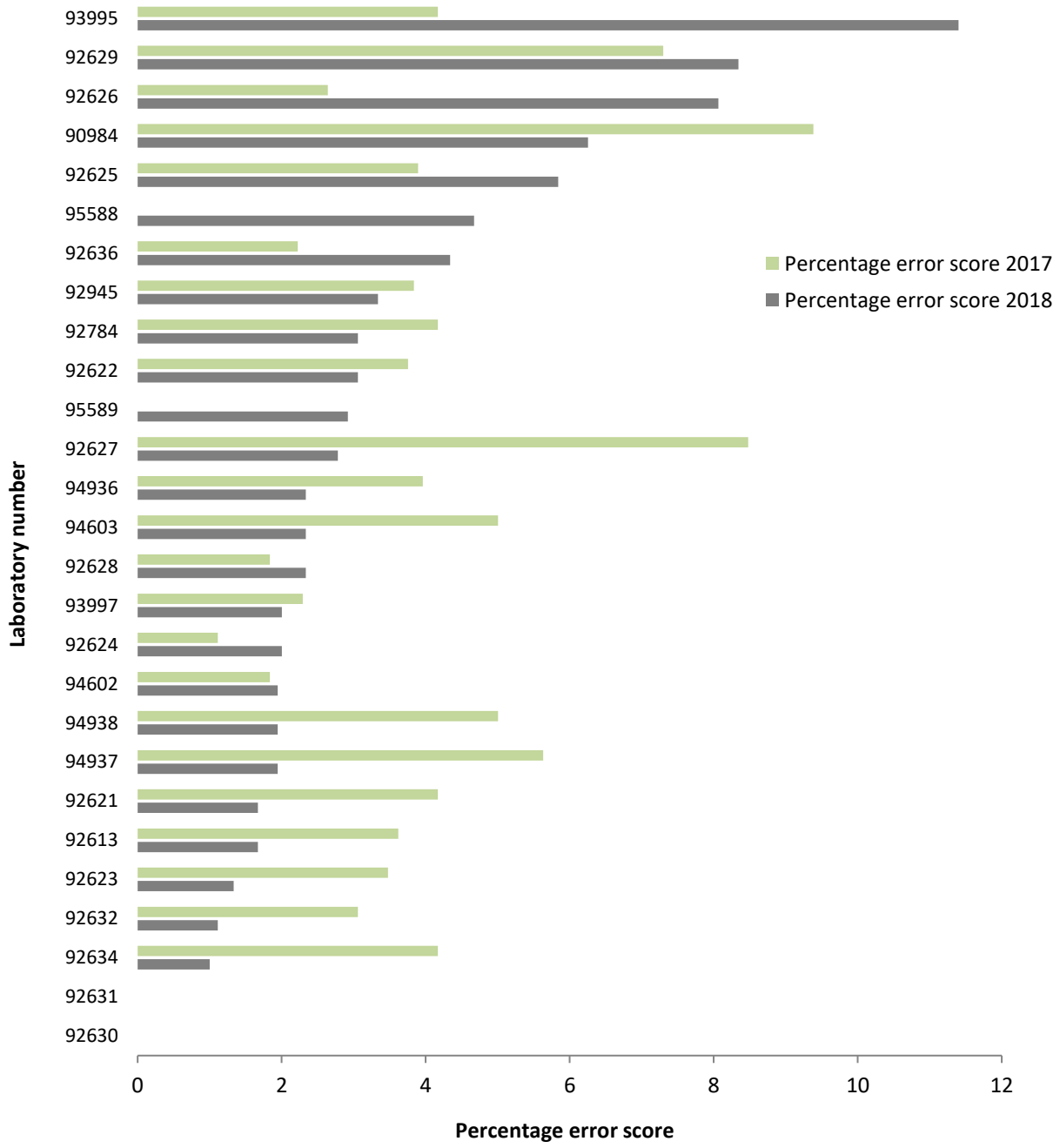


Note: The number of laboratories participating in the EQA changed over time: 18 laboratories (2010), 20 laboratories (2011), 19 laboratories (2012), 21 laboratories (2014), 26 laboratories (2015), 27 laboratories (2016), 28 laboratories (2017), 27 laboratories (2018)

3.7 Intralaboratory concordance

Intralaboratory concordance was examined using the triplicate (Strain 5) and two duplicate strains (Strains 1 and 4). Figure 4 shows the results for the 2018 EQA MIC values in comparison with the 2017 results. Most laboratories performed well, with 77.8% of laboratories (21/27) receiving a score of 5% or less, including two laboratories with a perfect score of zero. Of the six laboratories receiving a score of more than 5%, four had also received a score above 5% in the 2017 EQA. This issue is being investigated in collaboration with the affected laboratories. Fifteen of the 25 laboratories that participated in both the 2017 and 2018 EQA improved their internal concordance, and two remained the same with a perfect score of zero.

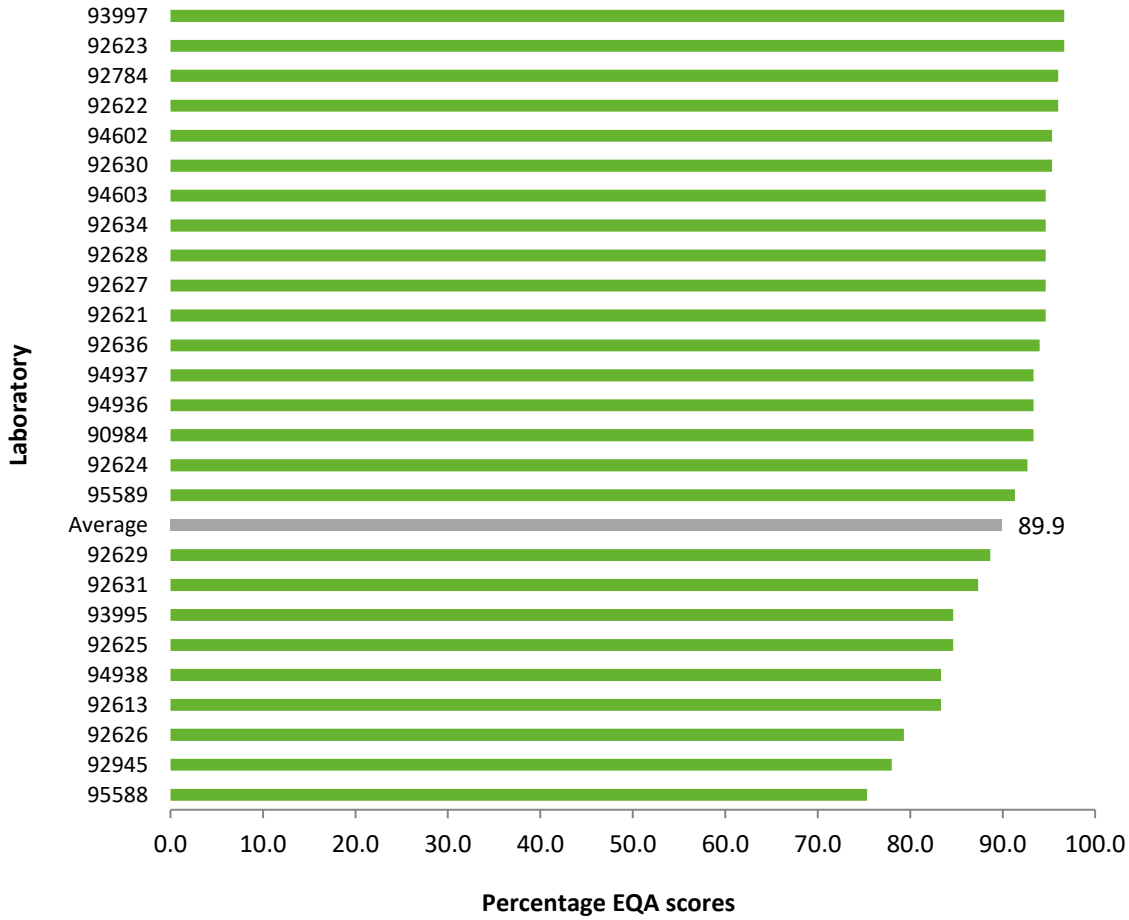
Figure 4: Intralaboratory MIC concordance error values, 2017 and 2018



3.8 Overall EQA scores

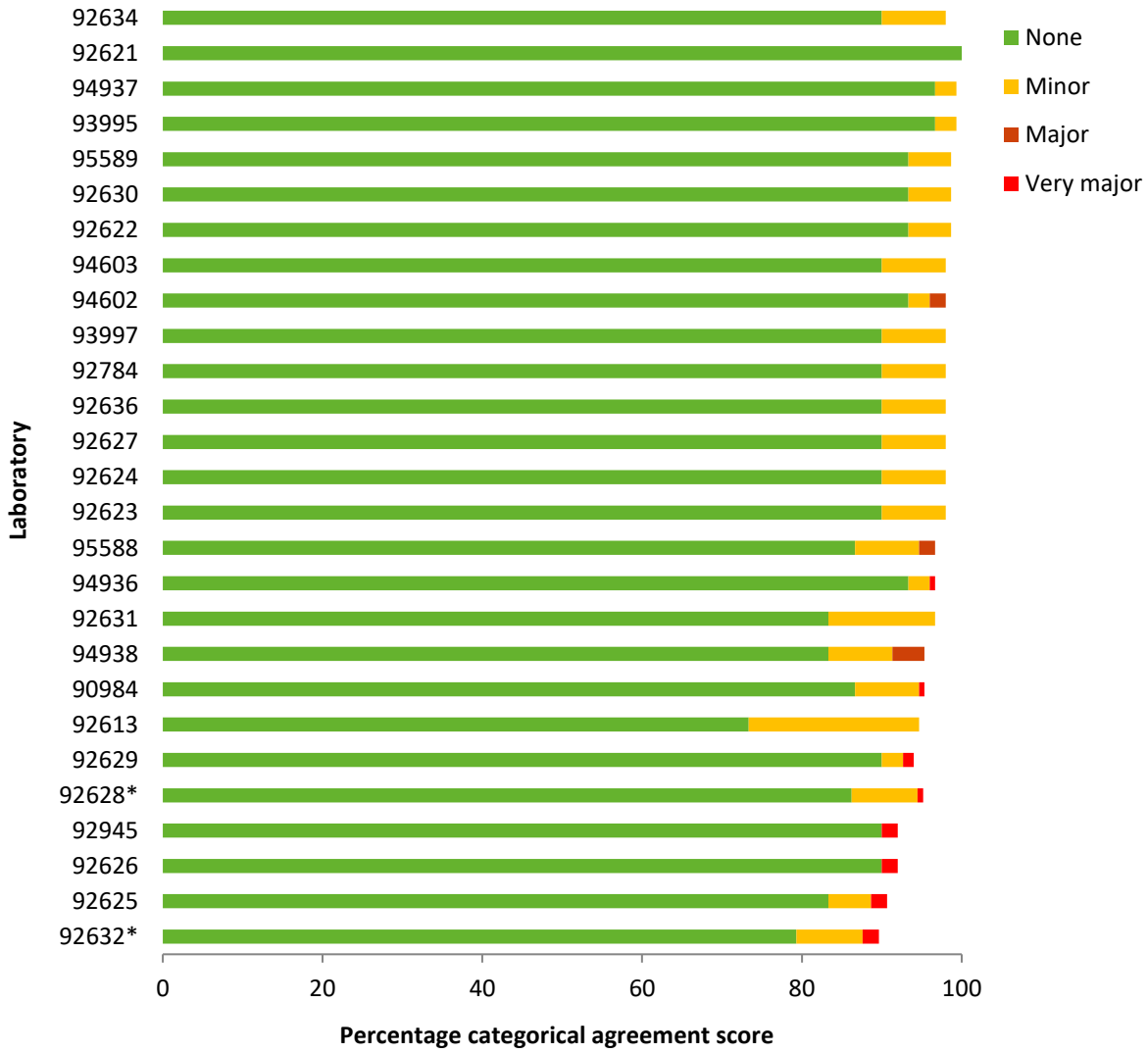
Figure 5 shows the overall MIC scores for the 2018 EQA, with the average score shown in grey (89.9%). Nine laboratories scored a below-average result. One of the below-average laboratories received a score above 5% – more than two doubling dilutions from the modal MIC.

Figure 5: EQA 2018 overall MIC scores



The scores for overall categorical agreement are shown in Figure 6. The total percentage score achieved by each laboratory out of a potential 150 is shown by the bars which are coloured to show the composition of the score by none, minor, major and very major faults.

Figure 6: EQA 2018 overall categorical agreement scores



** Laboratories 92628 and 92632 both had a potential maximum score of 145 rather than 150 as no SIR category was entered for one ciprofloxacin result.*

4 Discussion

The 2018 Euro-GASP EQA distribution was sent out to 27 laboratories in 26 participating countries, and all laboratories reported results for all, or almost all, of the requested tests. Most laboratories (96.3%) used MIC gradient strip tests to perform antimicrobial susceptibility testing in *N. gonorrhoeae*, which is higher than in the previous year. All participating laboratories used EUCAST guidelines to interpret MIC results, which points toward continuing harmonisation –EUCAST guidelines and MIC gradient strip tests are used across all Euro-GASP laboratories. The number of laboratories utilising chocolatised blood agar has increased from 32% in 2017 to 44% in 2018, while the number using GC agar base has decreased from 50% to 33%. From discussions with the laboratories that changed from using GC agar base, it appears this was largely due to supply issues, with only a limited number of suppliers providing the GC agar plates, combined with long delays between ordering plates and their arrival.

In general, the categorical agreement decreased for most antimicrobials in comparison with the previous distribution; the exception was ciprofloxacin, for which categorical agreement increased slightly (from 94.1% to 98.1%) and spectinomycin, which remained the same (100%). For ciprofloxacin, none of the strains had MICs close to a breakpoint, so the higher categorical agreement was not unexpected. The decreases for cefixime, ceftriaxone and beta-lactamase were negligible (below 4%), whereas the decrease for azithromycin was more notable at 10.5%. The reduction in concordance for azithromycin may be due to a higher proportion of strains in this distribution, with MICs close to breakpoints (six out of ten on breakpoint in 2018, three out of ten in 2017). Category of susceptibility agreed with the consensus (overall) assigned for each antimicrobial testing method in most cases. Discordant susceptibility category consensus results were due to the fact that the MICs of a few isolates were on, or near, breakpoints. For example, the modal azithromycin MIC for strains 4934, 4935 and 4938 were on the azithromycin intermediate breakpoint (MIC=0.25 mg/L), which resulted in discordant susceptibility category results. Overall, categorical agreement scores were high: only six laboratories received a score below 95%; three laboratories, however, had major faults, and eight had very major faults. The major and very major faults most commonly occurred in the azithromycin results due to the MICs around the breakpoints. Concordance of beta-lactamase detection also slightly decreased but still remained at a high level as for previous years. The choice of strains with MICs close to breakpoints will have an impact on category of susceptibility concordance. This highlights the need to consider the actual MIC of the isolates as well as susceptibility category when interpreting susceptibility results. It is important that reference laboratories have access to appropriate IQC strains such as the WHO control panel [3] to ensure their own quality assurance in a variety of diagnostic and antimicrobial susceptibility testing.

Essential MIC agreement was exceptionally high at 95.2%, an increase from the previous distribution (88.0%). The high level of essential agreement further supports the argument that the decrease in resistance category concordance was related to the high number of isolates with MICs close to breakpoints.

Breakdown of EQA susceptibility testing results by laboratory allowed for detailed analysis of individual laboratory performance. In the 2018 EQA, on the whole, laboratories performed well, with a good level of interlaboratory and intralaboratory concordance of results. However, one laboratory reported more than 5% variation from the modal MIC, but did have a low error value for intralaboratory results concordance. The issue appears to be confined to one antibiotic, ciprofloxacin, with a lower MIC achieved for three of the ten strains tested. Investigations to identify the root causes of these discrepancies are still ongoing, and further support to the laboratory is planned. In the 2017 EQA, seven laboratories reported more than 5% of results greater than two doubling dilutions from the modal MIC. Six of these have improved results in the QA18 EQA and have over 95% of results within two doubling dilutions of the modal MICs; this shows that the problems identified in QA17 have been rectified.

It should be noted that the methods for susceptibility testing as well as the breakpoints have changed over time, although there has been greater consistency in recent years. A full analysis on the different methods and breakpoints used in Euro-GASP EQAs over the years has recently been published [14].

5 Conclusion

The laboratories participating in the QA18 EQA scheme for susceptibility testing of *N. gonorrhoeae* showed good levels of competency and capability in recovering and testing strains of unknown phenotype. Inter- and intralaboratory concordance of categories of susceptibility for the different strains remained high, which strengthens confidence in Euro-GASP decentralised susceptibility testing and allows for meaningful comparisons with surveillance data from the members of the Euro-GASP network. These results indicate that the Euro-GASP antimicrobial susceptibility surveillance quality is of a good standard. The identification of results which are out of range trigger appropriate troubleshooting to ensure that the methodology being implemented is appropriate which in turn will lead to improvements in quality standards.

This Euro-GASP EQA is important to ensure that results from different submitting laboratories are comparable and that significant over- and underreporting of resistance does not occur. Antimicrobial susceptibility results from Euro-GASP contribute to the evidence base of gonorrhoea treatment guidelines, and local susceptibility testing can be used for individual patient management, so confidence in reporting is essential.

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Annex. QA18 detailed results

Table A1.1: Country coded category of susceptibility concordance – azithromycin

		Laboratory codes																														
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Total	No. sensitive	No. intermediate	No. resistant	Consensus	% Concordance
	4932	S	S	S	S	S	S	S	S	S	S	S	S	I	S	S	S	S	S	S	S	S	S	S	S	I	S	S						
1	4937	S	S	S	S	S	S	S	S	S	S	S	S	I	S	S	S	S	S	S	S	S	S	S	S	I	S	S	54	50	4	0	S	92.6
2	4933	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	27	0	0	27	R	100.0
3	4934	S	I	S	S	I	S	S	S	I	I	S	S	I	S	S	S	S	S	I	S	I	S	I	I	S	S	S	27	17	10	0	S	63.0
	4935	S	I	S	S	I	S	S	S	I	I	S	I	I	S	I	I	S	S	S	I	S	I	I	S	R	S	S						
4	4938	S	I	S	S	I	S	S	S	I	I	S	I	I	S	I	I	S	S	S	I	S	I	S	S	R	I	S	54	30	22	2	S	55.6
	4936	I	I	R	I	R	I	S	S	R	R	S	R	R	I	R	I	I	S	R	R	R	R	R	R	R	I	I						
	4939	I	I	R	R	R	I	S	S	R	R	S	R	R	I	R	R	I	S	R	R	R	R	R	R	R	I	I	81	12	25	44	R	54.3
5	4941	I	I	R	I	R	I	S	S	R	R	I	R	R	I	R	R	I	S	I	R	I	R	R	R	R	R	R						
6	4940	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	27	27	0	0	S	100.0
																																Total	77.6

Table A1.2: Country coded MIC values (mg/L) – azithromycin

		Laboratory codes																													
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
	4932	0.125	0.125	0.064	0.125	0.125	0.125	0.064	0.25	0.25	0.25	0.125	0.125	0.5	0.064	0.25	0.25	0.125	0.032	0.125	0.125	0.125	0.125	0.25	0.25	0.5	0.25	0.125					
1	4937	0.125	0.125	0.125	0.125	0.125	0.064	0.032	0.125	0.25	0.25	0.25	0.125	0.5	0.064	0.25	0.125	0.125	0.032	0.032	0.25	0.125	0.125	0.25	0.25	0.5	0.125	0.125	0.125	0.032	0.5	8	0
2	4933	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	≥256	0	0
3	4934	0.25	0.5	0.25	0.25	0.5	0.25	0.125	0.125	0.5	0.5	0.25	0.25	0.5	0.25	0.5	0.25	0.25	0.125	0.25	0.5	0.25	0.5	0.25	0.5	0.5	0.25	0.25	0.25	0.125	0.5	0	0
	4935	0.25	0.5	0.25	0.25	0.5	0.25	0.25	0.064	0.5	0.5	0.25	0.5	0.5	0.125	0.5	0.5	0.25	0.125	0.25	0.5	0.25	0.5	0.5	0.25	1	0.25	0.25					
4	4938	0.25	0.5	0.25	0.25	0.5	0.125	0.25	0.125	0.5	0.5	0.25	0.5	0.5	0.125	0.5	0.5	0.25	0.25	0.125	0.5	0.25	0.5	0.25	0.25	1	0.5	0.25	0.25	0.064	1	3	0
	4936	1	0.5	1	0.5	1	0.5	0.25	0.25	2	1	0.25	1	2	0.5	1	0.5	0.5	0.25	1	1	1	1	1	1	2	0.5	0.5					
	4939	1	1	1	1	1	0.5	0.25	0.25	2	1	0.25	1	2	0.5	1	1	0.5	0.25	1	1	1	1	0.25	1	2	0.5	0.5	1	0.125	2	11	1
5	4941	1	0.5	1	0.5	1	0.5	0.25	0.125	1	1	0.5	1	2	0.5	1	1	0.5	0.25	0.5	1	0.5	1	1	1	2	1	1					
6	4940	0.125	0.125	0.064	0.064	0.125	0.064	0.064	0.032	0.125	0.125	0.064	0.125	0.25	0.032	0.125	0.125	0.064	0.032	0.064	0.125	0.125	0.125	0.125	0.125	0.25	0.064	0.125	0.125	0.032	0.25	3	0

Table A1.3: Country coded category of susceptibility concordance – cefixime

		Laboratory codes																														
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Total	No. sensitive	No. intermediate	No. resistant	Consensus	% Concordance
	4932	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S						
1	4937	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	52	52	0	0	S	100.0
2	4933	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R	26	0	0	26	R	100.0
3	4934	R	R	R	R	R	R	R	S	S	R	R	S	R	S	R	R	R	R	R	R	S	R	S	R	N	S	26	7	0	19	R	73.1	
	4935	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S						
4	4938	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	N	51	51	0	0	S	100.0
	4936	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R						
	4939	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R	78	0	0	78	R	100.0
5	4941	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	R						
6	4940	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	26	26	0	0	S	100.0
																																Total	95.5

N – No result; not retrieved or susceptibility category not supplied

Table A1.4: Country coded MIC values (mg/L) – cefixime

		Laboratory codes																														
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
	4932	0.064	≤0.016	0.032	0.032	0.032	≤0.016	0.032	≤0.016	≤0.016	0.032	≤0.016	≤0.016	0.032	≤0.016	0.032	0.064	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	N	≤0.016					
1	4937	0.064	≤0.016	0.032	≤0.016	0.032	≤0.016	0.032	≤0.016	≤0.016	≤0.016	0.032	≤0.016	0.032	≤0.016	0.032	0.064	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	N	0.032	≤0.016	≤0.016	0.064	4	0
2	4933	4	2	2	2	2	2	2	1	1	2	2	1	2	1	4	1	2	1	2	1	2	2	2	N	1	2	1	4	0	0		
3	4934	0.5	0.25	0.5	0.25	0.25	0.25	0.5	0.125	0.125	0.25	0.25	0.125	0.25	0.064	0.5	0.5	0.5	0.25	0.25	0.25	0.25	0.125	0.25	0.125	0.25	N	0.125	0.25	0.064	0.5	1	0
	4935	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	0.032	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	N	≤0.016					
4	4938	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	N	≤0.016	≤0.016	≤0.016	0.032	0	0
	4936	2	2	2	1	2	1	2	1	1	2	1	1	2	1	2	1	2	1	2	1	1	0.5	1	1	2	N	1					
	4939	2	2	2	1	1	1	1	1	1	1	1	1	2	0.5	2	1	4	1	1	1	1	1	1	1	2	N	1	1	0.5	4	1	0
5	4941	2	2	2	1	2	1	2	1	1	2	1	1	2	0.5	2	1	2	1	0.5	1	1	0.5	1	1	2	N	1					
6	4940	≤0.016	≤0.016	<=0.01	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	<=0.01	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	N	≤0.016	≤0.016	≤0.016	≤0.016	0	0

Note: Laboratory 95588 did not submit cefixime data
N – no result; not retrieved, not tested or MIC not supplied

Table A1.5: Country-coded category of susceptibility concordance – ceftriaxone

		Laboratory codes																														
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Total	No. sensitive	No. intermediate	No. resistant	Consensus	% Concordance
	4932	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
1	4937	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	54	54	0	0	S	100.0
2	4933	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	27	0	0	27	R	100.0
3	4934	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	R	S	27	26	0	1	S	96.3
	4935	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
4	4938	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	54	54	0	0	S	100.0
	4936	R	R	R	R	R	R	R	R	R	S	R	R	R	S	R	R	R	R	R	R	R	R	R	R	R	R	R						
	4939	R	R	R	R	R	R	R	R	R	R	R	R	R	S	R	R	R	R	R	R	R	R	R	R	R	R	R	81	4	0	77	R	95.1
5	4941	R	R	R	R	R	R	R	R	R	R	R	R	R	S	R	R	R	R	R	R	R	R	R	R	R	R	R						
6	4940	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	27	27	0	0	S	100.0
																																Total	98.6

Table A1.6: Country coded MIC values (mg/L) – ceftriaxone

		Laboratory codes																														
	Strain	90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
	4932	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	≤0.016					
1	4937	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	0	0
2	4933	0.5	0.5	0.5	0.5	1	0.5	1	0.5	0.5	0.5	1	0.5	0.5	0.25	0.5	0.5	1	0.5	0.5	0.5	0.5	1	0.5	0.5	0.5	2	0.25	0.5	0.25	2	2	0
3	4934	0.125	0.064	0.125	0.064	0.125	0.064	0.125	0.032	0.064	0.125	0.125	0.064	0.064	0.064	0.064	0.064	0.125	0.064	0.064	0.064	0.125	0.064	0.064	0.032	0.064	0.25	0.032	0.064	0.016	0.25	2	0
	4935	≤0.016	≤0.016	0.032	≤0.016	≤0.016	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.032	0.032	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.064	≤0.016					
4	4938	≤0.016	≤0.016	0.032	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0.064	≤0.016	≤0.016	≤0.016	0.064	2	0
	4936	0.5	0.25	1	0.25	0.5	0.5	0.5	0.25	0.5	0.5	0.5	0.5	0.5	0.125	0.5	0.25	0.5	0.5	0.25	0.5	0.5	0.25	0.25	0.25	0.5	2	0.25					
	4939	0.5	0.25	1	0.25	0.5	0.5	0.5	0.25	0.5	0.5	0.5	0.5	0.5	0.125	0.5	0.25	0.5	0.25	0.25	0.5	0.5	0.25	0.25	0.25	0.25	1	0.25	0.5	0.125	2	4	0
5	4941	0.5	0.25	1	0.25	0.5	0.5	0.5	0.25	0.5	0.5	0.25	0.5	0.5	0.125	0.5	0.25	0.5	0.5	0.25	0.5	0.5	0.25	0.25	0.25	0.25	1	0.25					
6	4940	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	≤0.016	0	0

Table A1.7: Country coded category of susceptibility concordance – ciprofloxacin

	Strain	Laboratory codes: 90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Total	No. sensitive	No. intermediate	No. resistant	Consensus	% Concordance
	4932	R	I	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	54	1	2	51	R	94.4
1	4937	S	I	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
2	4933	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	27	0	0	27	R	100.0
3	4934	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	27	0	0	27	R	100.0
	4935	S	S	S	S	S	S	I	S	S	S	S	S	S	S	S	S	S	S	S	S	R	S	S	S	S	S	S	54	51	2	1	S	94.4
4	4938	S	S	S	S	S	S	I	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S						
	4936	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	80	0	0	80	R	100.0
	4939	R	R	R	R	R	R	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
5	4941	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R						
6	4940	S	S	S	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	26	26	0	0	S	100.0
																													Total					98.1

Table A1.8: Country coded MIC values (mg/L) – ciprofloxacin

	Strain	Laboratory codes: 90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
	4932	0.064	0.064	0.5	0.5	0.5	1	0.5	0.5	0.5	0.5	1	1	0.5	0.25	1	>0.06	0.5	0.5	0.25	0.5	0.5	1	0.5	1	1	0.5	0.25	0.5	0.064	1	0	3
1	4937	0.5	0.064	0.5	0.5	0.5	1	0.5	0.25	1	0.5	0.5	1	0.5	0.25	1	>0.06	0.5	0.5	0.25	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.25					
2	4933	8	4	≥32	≥32	≥32	≥32	16	≥32	≥32	16	≥32	≥32	8	4	≥32	>0.06	≥32	8	8	≥32	≥32	≥32	≥32	16	16	8	8	≥32	4	≥32	0	2
3	4934	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	>0.06	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	>0.06	≥32	0	0
	4935	0.008	0.004	0.008	0.008	0.008	0.016	0.008	0.004	0.008	0.008	0.016	0.016	0.008	0.004	0.008	<0.06	0.008	0.008	0.004	0.004	0.008	0.008	0.008	0.008	0.008	0.008	0.008	0.008	0.002	0.016	0	0
4	4938	0.008	0.004	0.008	0.008	0.008	0.016	0.008	0.004	0.008	0.008	0.008	0.016	0.008	0.004	0.008	<0.06	0.008	0.008	0.002	0.008	0.008	0.008	0.008	0.008	0.008	0.008	0.008					
	4936	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	>0.06	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	>0.06	≥32	0	0
	4939	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	>0.06	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32					
5	4941	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	>0.06	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32	≥32					
6	4940	0.002	0.002	0.002	0.002	0.002	0.004	0.002	0.002	0.002	0.004	0.004	0.004	0.002	0.002	0.002	<0.06	0.002	0.004	0.002	0.002	0.002	0.002	0.002	0.004	0.002	0.002	0.002	0.002	0.002	0.004	0	0

Table A1.9: Country coded category of susceptibility concordance – spectinomycin

	Strain	Laboratory codes: 90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Total	No. sensitive	No. intermediate	No. resistant	Consensus	% Concordance
	4932	N	N	S	S	S	N	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N	38	38	0	0	S	100.0
1	4937	N	N	S	S	S	N	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N						
2	4933	N	N	S	S	S	N	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N	19	19	0	0	S	100.0
3	4934	N	N	S	S	S	N	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N	19	19	0	0	S	100.0
	4935	N	N	R	R	R	N	R	R	R	R	N	N	R	R	R	R	R	R	R	N	R	R	N	R	R	R	N	38	0	0	38	R	100.0
4	4938	N	N	R	R	R	N	R	R	R	R	N	N	R	R	R	R	R	R	R	N	R	R	N	R	R	R	N						
	4936	N	N	S	S	S	N	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N						
	4939	N	N	S	S	S	N	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N	57	57	0	0	S	100.0
5	4941	N	N	S	S	S	N	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N						
6	4940	N	N	S	S	S	N	S	S	S	S	N	N	S	S	S	S	S	S	S	N	S	S	N	S	S	S	N	19	19	0	0	S	100.0
																													Total					100.0

N – not retrieved or susceptibility category not supplied.

Table A1.10: Country coded MIC values (mg/L) – spectinomycin

	Strain	Laboratory codes: 90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different	>2 dilutions different
	4932	N	N	32	8	32	N	16	4	16	16	N	N	32	8	16	64	16	16	8	N	16	16	N	16	16	16	N	16	4	64	2	0
1	4937	N	N	32	8	32	N	8	4	16	16	N	N	32	8	16	64	16	16	8	N	16	16	N	16	16	16	N					
2	4933	N	N	16	4	16	N	16	4	16	16	N	N	16	8	16	64	16	16	8	N	16	16	N	16	16	8	N	16	4	64	2	0
3	4934	N	N	32	8	16	N	8	8	16	16	N	N	16	8	16	64	16	16	8	N	16	8	N	16	16	8	N	16	8	64	0	0
	4935	N	N	>128	≥1024	≥1024	N	≥1024	≥1024	≥1024	≥1024	N	N	≥1024	≥1024	≥1024	≥1024	≥1024	>128	≥1024	N	≥1024	≥1024	N	≥1024	≥1024	≥1024	N	≥1024	>128	≥1024	0	0
4	4938	N	N	>128	≥1024	≥1024	N	≥1024	≥1024	≥1024	≥1024	N	N	≥1024	≥1024	≥1024	≥1024	≥1024	>128	≥1024	N	≥1024	≥1024	N	≥1024	≥1024	≥1024	N					
	4936	N	N	32	4	16	N	8	8	16	8	N	N	16	8	16	64	16	16	16	N	16	8	N	16	8	8	N					
	4939	N	N	32	8	16	N	16	8	16	8	N	N	16	8	16	64	8	16	8	N	16	8	N	8	8	8	N	16	2	64	1	1
5	4941	N	N	32	8	16	N	16	2	16	8	N	N	16	8	16	64	16	16	16	N	16	8	N	16	8	8	N					
6	4940	N	N	16	8	16	N	16	4	16	16	N	N	16	8	16	64	8	16	16	N	16	8	N	8	8	8	N	16	4	64	1	0

Note: Laboratories 90984, 92613, 92624, 92629, 92630, 93997, 94936 and 95589 did not submit spectinomycin data
N – no result; not retrieved, not tested or MIC not supplied

Table A1.11: Country coded MIC values (mg/L) – gentamicin

	Strain	Laboratory codes: 90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Modal MIC	Min MIC	Max MIC	2 dilutions different
	4932	N	N	8	4	N	4	4	4	8	N	N	8	16	2	N	N	8	N	4	4	4	N	8	8	8	4	N	4	2	16	4
1	4937	N	N	16	4	N	4	4	4	16	N	N	8	16	2	N	N	8	N	4	4	4	N	4	8	8	4	N				
2	4933	N	N	8	4	N	4	2	4	8	N	N	8	8	2	N	N	8	N	4	2	4	N	4	8	8	4	N	8	2	8	3
3	4934	N	N	8	4	N	4	4	2	8	N	N	8	4	2	N	N	4	N	4	2	4	N	4	8	8	4	N	4	2	8	0
	4935	N	N	8	4	N	4	4	2	16	N	N	16	8	2	N	N	2	N	4	4	8	N	4	8	8	8	N	4	2	16	4
4	4938	N	N	8	4	N	2	4	4	16	N	N	16	8	2	N	N	4	N	4	4	4	N	4	8	8	8	N				
	4936	N	N	8	4	N	4	2	4	8	N	N	8	8	2	N	N	4	N	4	4	4	N	4	4	8	4	N				
5	4939	N	N	8	4	N	4	4	8	8	N	N	8	8	2	N	N	4	N	4	2	4	N	2	4	8	2	N	4	2	8	0
	4941	N	N	8	4	N	4	4	2	8	N	N	8	8	2	N	N	4	N	2	2	4	N	2	4	8	4	N				
6	4940	N	N	8	4	N	4	4	4	8	N	N	8	8	2	N	N	4	N	4	4	4	N	4	16	8	4	N	4	2	16	1

Note: Laboratories 90984, 92613, 92623, 92628, 92629, 92634, 92636, 92945, 94603, and 95589 did not submit gentamicin data
N – no result; not retrieved, not tested or MIC not supplied

Table A1.12: Country coded concordance – beta-lactamase

	Strain	Laboratory codes: 90984	92613	92621	92622	92623	92624	92625	92626	92627	92628	92629	92630	92631	92632	92634	92636	92784	92945	93995	93997	94602	94603	94936	94937	94938	95588	95589	Total	No. sensitive	No. intermediate	No. resistant	Consensus	% Concordance
	4932	R	R	R	R	R	R	S	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	S	R	R	N	50	3	0	47	R	94.0
1	4937	R	R	R	R	R	R	R	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	S	R	R	N						
2	4933	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	25	25	0	0	S	100.0
3	4934	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	25	25	0	0	S	100.0
	4935	S	R	R	R	R	R	R	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	N	50	2	0	48	R	96.0
4	4938	R	R	R	R	R	R	R	R	R	R	N	R	R	R	R	R	R	R	R	R	R	R	R	S	R	R	N						
	4936	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	R	S	S	S	N						
	4939	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	R	S	S	S	N	75	72	0	3	S	96.0
5	4941	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	R	S	S	S	N						
6	4940	S	S	S	S	S	S	S	S	S	S	N	S	S	S	S	S	S	S	S	S	S	S	S	S	S	S	N	25	25	0	0	S	100.0
																													Total					97.7

Note: Laboratories 92629 and 95589 did not submit any beta-lactamase testing results
N – No result; not retrieved or beta-lactamase result not supplied

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